Paediatric antimicrobial utilization in a tertiary hospital in north central Nigeria

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ABSTRACT

Background: The use of antimicrobials has been on the rise among paediatric patients in Nigerian clinical settings, possibly due to increased prevalence of infectious diseases among this age group. Inappropriate use of antimicrobials can pose a serious threat to life due to the development of antimicrobial drug resistance.

Objectives: To determine antimicrobial prescription pattern among paediatric patients and to evaluate compliance with WHO core prescribing indicators and calculated Indices of Rational Drug Prescribing (IRDP).

Methods: A retrospective, cross sectional study which extracted data from folders of paediatric patients who were admitted in Federal Medical Center, Makurdi, Benue State, Nigeria from January 2019 to December 2019, was carried out using a well-designed proforma. Data was analysed using International Business Machine (IBM) version 23 and presented in form of simple percentages and charts.

Results: Most of the prescriptions were within normal doses (74.6%). Unasyn® (Ampicillin/Sulbactam) was the most prescribed antibiotics (16.2%). Comparing with WHO core prescribing indictors, the average number of drugs per encounter was 2.1 as against 1.6-1.8. Calculated Indices of Rational Drug Prescribing (IRDP) was 3.03 as against the ideal IRDP of 5. Compliance with standard prescription writing format was high, except for the Physician's name, which more than 50% of the prescriptions did not have.

Conclusion: The most prescribed antimicrobial agent was ampicillin/sulbactam. Compliance with standard prescribing format was reasonably high but needs improvement. Compliance with WHO core prescribing indicators was poor except for generic prescribing and prescribing from EMDEX. Generally, polypharmacy was observed. IRDP was low in this research at 3.03.

Keywords: Paediatric, antimicrobial utilization, irrational drug prescribing, antimicrobial drug resistance.

Utilisation pédiatrique des antimicrobiens dans un hôpital tertiaire du centre-nord du Nigéria

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RÉSUMÉ

Contexte : L'utilisation d'antimicrobiens est en hausse chez les patients pédiatriques dans les milieux cliniques nigérians, probablement en raison de la prévalence accrue des maladies infectieuses dans cette tranche d'âge. L'utilisation inappropriée d'antimicrobiens peut constituer une grave menace pour la vie en raison du développement de la résistance aux médicaments antimicrobiens.

Objectifs : Déterminer le modèle de prescription d'antimicrobiens chez les patients pédiatriques et évaluer la conformité avec les indicateurs de prescription de base de l'OMS et les indices calculés de prescription rationnelle des médicaments (IRDP).

Méthodes : Une étude rétrospective transversale qui a extrait des données de dossiers de patients pédiatriques qui ont été admis au Federal Medical Center, Makurdi, Benue State, Nigeria de janvier 2019 à décembre 2019, a été réalisée à l'aide d'un formulaire bien conçu. Les données ont été analysées à l'aide de la version 23 d'IBM (International Business Machine) et présentées sous forme de pourcentages simples et de graphiques.

Résultats : La plupart des prescriptions étaient conformes aux doses normales (74,6 %). Unasyn® (Ampicilline/Sulbactam) était l'antibiotique le plus prescrit (16,2%). Par rapport aux indicateurs de prescription de base de l'OMS, le nombre moyen de médicaments par consultation était de 2,1 contre 1,6-1,8. Les indices calculés de prescription rationnelle des médicaments (IRDP) étaient de 3,03 par rapport à l'IRDP idéal de 5. Le respect du format standard de rédaction des ordonnances était élevé, à l'exception du nom du médecin, qui ne figurait pas sur plus de 50 % des ordonnances.

Conclusion : L'agent antimicrobien le plus prescrit était l'ampicilline/sulbactam. La conformité au format de prescription standard était raisonnablement élevée mais doit être améliorée. La conformité aux indicateurs de prescription de base de l'OMS était faible, sauf pour la prescription de médicaments génériques et la prescription à partir d'EMDEX. En général, la polypharmacie a été observée. L'IRDP était faible dans cette recherche à 3,03.

Mots clés : Pédiatrie, utilisation des antimicrobiens, hôpital tertiaire

INTRODUCTION

Antimicrobials, particularly antibiotics, are one of the predominant medications used in paediatric populations in hospital settings.[1] Several studies have shown that the average proportion of children who receive at least one antibiotic in the hospital setting ranges from 33% to 78%.[2,3,4] Antimicrobial agents are used for therapy either empirically, definitively or prophylactically.[5]

It is an observed fact that communicable diseases are the major causes of morbidity and mortality among the young population in Nigeria. These infections, whether Community Acquired (CAI) or Hospital Acquired (HAI), play a major contributory role in antimicrobial use on the wards. Aside communicable diseases, the presence of comorbidities among paediatric patients may be linked to increased or over prescribing of antimicrobial agents.

The judicious and rational use of antimicrobials is an integral part of good clinical practice as it maximises therapeutic efficacy.[6] However, irrational and excessive use of these agents has become a global challenge. Several publications have attested to the fact that overuse or inappropriate use of antimicrobials can increase the emergence of resistance.[6,7]

Irrational use of antimicrobials can result in resistance and poor treatment outcomes, be it Economic, Clinical and/or Humanistic Outcomes (ECHO). Antimicrobial resistance is a global challenge as it compromises the effectiveness of infectious diseases management.[8] It further worsens treatment outcomes by increasing virulence, cost and length of hospitalisation, and limiting treatment options with resultant increase in morbidity and mortality. There is, therefore, need to drive antimicrobial stewardship, and to draw up a policy document on appropriate use of antimicrobials in order to address the threat of drug resistance.

An online search has shown that there is, paucity of data on antimicrobial use in the hospital, especially among paediatric populations, evidenced by lack of published work on paediatric antimicrobial utilisation in the study setting. This research studied the antimicrobial prescription pattern in paediatrics, with the aim of providing a baseline data that would serve as an informed tool for developing a policy document for antimicrobial use in the hospital following the institution of antimicrobial stewardship programme in the organisation. It also sought to evaluate compliance with WHO core prescribing indicators and calculated Indices of Rational Drug Prescribing (IRDP).

METHODS

Research setting

This study was conducted at the Federal Medical Center, Makurdi, Benue State, Nigeria: a tertiary Hospital located in Makurdi metropolis with sites across all the geopolitical zones in the state. The center is a 400-bedded hospital with different departments, including Paediatrics, Obstetrics and Gynaecology (O&G), Pharmacy, Internal Medicine, Surgery, Nursing, Laboratory Sciences, Ophthalmology, Radiology, Optometrics, Dentistry, Dietetics, Clinical Psychology Departments rendering clinical services and other departments offering support services. The Paediatric department comprises of the Special Care Baby Unit (SCBU), Emergency Paediatric Unit, Children's ward and Orthopaedic Paediatric Ward.

Research design and sampling

A retrospective cross-sectional study was used to assess antimicrobial utilisation in the paediatric ward from January to December 2019. Medical records of paediatric Patients (Children < 14 years of age) who were admitted in the paediatric ward of the Hospital were used to assess antimicrobial utilisation pattern. Systematic random sampling (where one out of every nine (9) case files were selected) was used to select records, using a sampling frame from paediatric records from January 2019 to December 2019. From a population of 3336, as obtained from the records department, a sample size of 357 was derived, using Taro Yamane's formula for sample size calculation as shown by Raphael, 2014.[9] However, due to misfiling and missing data, only 180 of the case files met the inclusion criteria, hence, were used for data extraction.

Only records of paediatric patients who had a minimum of three consecutive days of hospitalization with not more than three missing data were included.

Data collection and analysis

A checklist designed for data collection was used to extract data. Three pharmacists who had been trained on the use of the data collection instruments extracted the required data. Monitoring was done daily by the Principal Investigator to ensure data quality. Descriptive statistics: Simple percentages and means were used to analyse data. Data were also presented in the form of charts.

Ethical consideration

The approval of the Hospital Research Ethical Committee (HREC) was obtained and confidentiality of patient

records ensured.

RESULTS

Only 180 patients' folders that met the inclusion criteria were included in the study. Of this number, 103 (57.2%) patients' folders were obtained from the Emergency Paediatrics Unit (EPU), while 77 (42.8%) patients' folders were obtained from the Special Care Baby Unit (SCBU).

As shown in Table 1, out of the 180 cases studied, 102 (56.7%) were males, 91 (50.6%) were below one month of age, 34 (18.9%) were between 1-12 months, while 44 (24.4%) were above 24 months. A total of 55 (30.6%) of the cases were below 2.5kg in weight, while eight (4.4%) were above 15kg.

The most prevalent condition was sepsis, with 86 (47.8%) cases of occurrence while the least occurring infectious disease condition was Measles/Mumps Disease (MD) with a prevalence of 13 (7.2%). Three (7%) of the cases had no diagnosis. See Table 2.

As shown in Figure 1, majority of the prescriptions had complete patient biodata (98.5%). While 87.4% of the prescriptions had signatures of physicians, only 40.3% had the names of the physicians. Generic prescribing was 74% and dose appropriateness, based on child's weight and age, was 74.6% of the total prescriptions.

The total number of antimicrobial agents' type prescribed during this study was 10. Majority of these antimicrobial agents were administered via the intravenous (IV) route. IV Ampicillin + Sulbactam (Unasyn®) was the most prescribed antibiotics at 64 (16.2%), while Cefotaxime was the least prescribed 20 (5.0%) agent as shown in Table 3.

Figure 2 shows that out of all the prescriptions encountered, only 19.4% had one antimicrobial agent prescribed. About 42.8% contained two antimicrobial agents, while the rest contained in a range of three to five antibiotics with 2.8% of the prescriptions having no antimicrobial agents.

Other details are as shown in the Tables/Figures below:

Table 1: Socio-demographic characteristics (n=180)

Variable	Frequency	Percentage
Age(in months)		
<1 month	91	50.6
1-12 months	34	18.9
13-24months	11	6.1
>24 months	44	24.4
Gender		
Male	102	56.7
Female	78	43.3
Weight		
<2.5	55	30.6
2.5-5.9	49	27.2
6-10.9	36	20.0
11-15	32	17.8
>15	8	4.4
Source of prescription orders		
EPU	103	57.2
SCBU	77	42.8

EPU=Emergency Paediatric Unit, SCBU= Special Care Baby Unit

Table 2: Diagnosis pattern (n=180)

Variable	Frequency	Percentage
Diagnosis		
Sepsis	86	47.8
Intra-abdominal malignancy	22	12.2
Meningitis	34	18.9
Urinary Tract Infections	22	12.2
Measles/Mumps Disease	13	7.2
No diagnosis	3	1.7

Prescription pattern

% with Doctor's signature — 87.4
% with Doctor's Name — 40.5
% with Date of Prescription — 97.2
% with full patients biodata — 98.5
% with generic names — 74
% with correct doses — 74.6

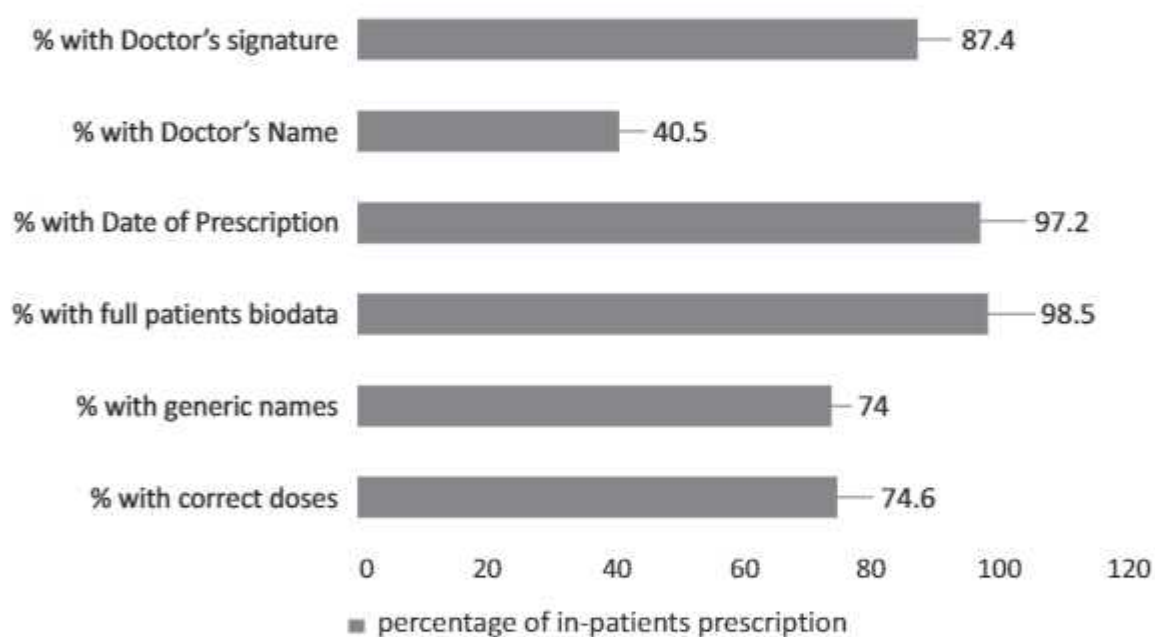(x-axis: 0, 20, 40, 60, 80, 100, 120)

■ percentage of in-patients prescription

Figure 1: compliance with standard prescription writing format

Table 3: Distribution of the prescribed antibacterial drugs

Drug Category	Frequency	Percentage
Unasyn®	64	16.2
Ceftriaxone	58	14.7
Meropenem	42	10.6
Ceftazidime	41	10.4
Fluconazole	37	9.4
Gentamycin	37	9.4
Tandak®	36	9.1
Ciprofloxacin	27	6.8
Metronidazole	33	8.4
Cefotaxime	20	5.0

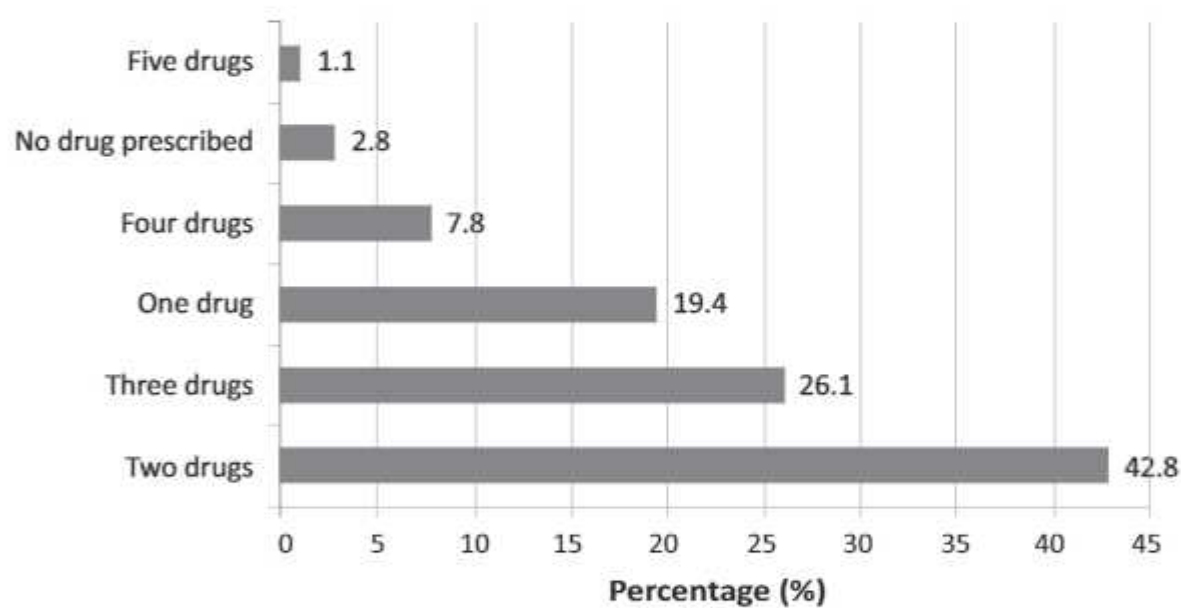*Note: Patient may receive more than one drug in each prescription*

Figure 2: Number of drugs per prescription

Table 4: WHO core prescribing indicators assessed for drug prescriptions

S/N	Prescribing indicators	Encounters	Average/ percentage	Previously derived in Nigeria[10]	WHO standard derived or ideal
1	Drugs per encounter	395 (total)	2.1 (average)	3.8	1.6-1.8
2	Percentage of drugs prescribed with generic name	295	74%	58%	100%
3	Encounters with any antibiotic(s) prescribed	392	99.2%	48%	20%-20.6%
4	Encounters with injections	395	100%	37%	13.4%-24.1%
5	Percentage on EMDEX	395	100%		100%

Extracted from

Table 5: Calculated indices of rational drug prescribing (IRDP)

Non-Polypharmacy	Generic prescribing	Rational antibiotic prescribing	Rational injection prescribing	Essential drug index	IRDP* (total)	Ideal IRDP**
0.85	0.74	0.20	0.24	1	3.03	5.0

* Calculated IRDP for this study
** Ideal (WHO) IRDP

DISCUSSION

This study sought to assess the antimicrobial prescription pattern of physicians among paediatric patients' population, and to evaluate compliance with the WHO core prescribing indicators and IRDP.

The study found a high rate of antibiotics use for children, the majority of who were aged 5 years and below, being also predominantly male, admitted in the paediatric wards. The predominance of the younger age group could be a reflection of the larger infectious diseases burden among under 5 children,[11] warranting the use of antibiotics. There was also a male preponderance found, which has similarly being observed in previous reports of studies on prescriptions for children admitted in the North-west region of India, Nigeria, Sierra Leone[13] and Ethiopia.[12-15] It is not clear in our study, the reason for the male preponderance in the population of children that received the prescriptions over the study period, but male child preference (and selective priority in care for children) as suggested in previous studies,[14-16] may be the reasons in the communities served by the facility studied.

Although the majority of antibiotic prescriptions were found to be accurate in dosage per unit body weight (kg), an appreciable proportionate dose outside the recommended ranges as provided in both the 2010-2011 British National Formulary for children and the 2013 Emdex Paediatric Drug Guide used in Nigeria[17] were observed. Use of higher doses has implications for safety, with a tendency to cause dose-dependent side-effects, drug resistance and adverse drug reactions. Conversely, use of insufficient doses than the recommended could lead to development of antimicrobial resistance, poor

therapeutic response, and treatment failure. These may ultimately lead to decision to change antibiotics, thereby, adding more costs and prolongation of treatment.

A proportion of close to one-half of all prescriptions orders containing antibiotics in this study is suggestive of evidence of unnecessary antibiotic use, being over twice as much as the WHO recommended standard. Anyanwu and Arigbe-Osula (2012), reported the presence of antibiotics in up to 63.3% - 86.6% of inpatients prescriptions of admitted children in a tertiary hospital in South-eastern Nigeria,[18] whereas, Cole *et al.*, 2015 reported up to 74.8% of prescriptions containing antibiotics.[13] It could be reasonable to presume that children (especially under-fives) in this study could have received more antibiotics in their prescriptions as a consequence of their vulnerability to infectious diseases, which has been recognised in global epidemiology of child morbidity and mortality.[11]

The rate of injection use was about thrice the WHO recommended and about twice the previously obtained value in Nigeria.[10] The tendency for use of more injections than the ideal is evidence of irrational medicines' use of a public health concern. Apart from its potential to generate hazardous waste, it predisposes to unwarranted pain, promotes the spread of blood-borne infections, development of complications, and promotes microbial resistance. Irrational prescribing of antibiotics and injections increases health-care costs and adds extra strain on the already weak health infrastructure and human resources. In this study, injections were prescribed more than necessary with average percentage of 100% (IRDP of 0.24) of all prescriptions having at least an injection. Anyanwu and Arigbe-Osula (2012) also reported 80% -86% of drugs administered parenterally among paediatric inpatients in a tertiary hospital, with 80-85% of drugs prescribed from the hospital formulary.[18] Comparatively, lower injections prescribing rates of 20% were noted in a similar study among admitted children in Sierra Leone, 13 but the rates were up to 96% in Pakistan.[19] Table 4, gives a summary of these indicators side by side with previously derived values obtained from studies in Nigeria[10] compared with the WHO/Ideal standards. The high level of injection use in these patients may be attributed to the seriousness of their illnesses, being patients admitted in the Special Care Baby Unit (SCBU) and Emergency Paediatric Unit (EPU). Meanwhile the mean number of drugs per prescription was 2.1 implying over prescribing which has its consequences of increased drug therapy problems, increased cost, poor

adherence and higher chances of developing drug resistance.

IRDP is an indicator used to measure rational drug use. The IRDP as obtained from the component indices in this study was suboptimal (3.03), compared to the ideal IRDP (5.0). This implies irrational antibiotics prescribing. Injection and antibiotic prescribing had the lowest scores (0.24 and 0.20, respectively) while essential drug index had the highest index score (1). This result was slightly higher than the result from another study carried out in Nigeria, which showed a total IRDP number of 2.99.[10]

The finding of almost a quarter of all prescription orders that contained four or five drugs suggest a tendency for polypharmacy in the prescribing habits that prevailed in the facility. Furthermore, an average of 2.1 drugs prescribed per patient encounter, being higher than the WHO recommended standard range of 1.6-1.8, is further evidence of that tendency for polypharmacy. The value is, however, much lower than a previously derived finding (3.8) from an earlier study (in Nigeria) that also established the recommended average for developing countries. Although the WHO standard value was obtained largely from adult outpatient settings across developing countries (with fewer paediatric prescriptions),[10] they remain the only valid reference standards available for such comparison. Compared to what was reported in similar studies in Ethiopia, Sierra Leone, Nigeria, and India.[12,13,19,20] the average of 2.1 drugs per encounter in this study is the lowest, even though just slightly above the WHO standard. The difference between the finding in this study and these cited reports could, however, be attributed to differences in study methodology. Polypharmacy could potentially predispose to higher risk of antimicrobial resistance, drug-drug interactions and other adverse events. Similarly, redundant medicines within a prescription and use of brand names can add to the financial burden on patients and health-care resources.[10]

CONCLUSION
This study provided a baseline information on rational prescribing of antimicrobials for children admitted into the hospital. The prescribed antibiotics of highest prevalence was ampicillin+sulbactam combination (Unasyn®) followed by ceftriaxone while the least was cefotaxime. Compliance with WHO core prescribing indicators was poor except for prescribing from EMDEX and slightly, generic prescribing. Generally, poly-pharmacy was observed as most of the prescriptions had

2 antibiotics or more with a documented low IRDP.

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